Case Creation Option

Case "10544281" already exists. Please overwrite it or cancel the operation.

The Contents of Case *"10544281"*

Qnum	Query	DB Name	Thesaurus	Operator	Plural
Q1	avermectin	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q2	Q1 and saccharide	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q3	Q2 and monosaccharide	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q4	pesticide	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q5	Q4 and Q1	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q6	Q5 and Q2	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q7	Q6 and Q3	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q8	549/264	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q9	Q8 and ll2	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q10	Q8 and Q2	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q11	514/30	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q12	Q11 and Q2	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q13	514/450	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q14	Q13 and Q2	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q15	Q14 and Q3	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES
Q16	Q3 and Q12	PGPB,USPT,USOC,EPAB,JPAB,DWPI	None	ADJ	YES

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WEST Search History

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DATE: Saturday, February 04, 2006

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L1	avermectin	2637
☐	L2	L1 and saccharide	108
☐	L3	L2 and monosaccharide	36
☐	L4	pesticide	50737
☐	L5	L4 and l1	859
☐	L6	l5 and l2	18
☐	L7	l6 and l3	7
☐	L8	549/264	250
☐	L9	L8 and l12	0
☐	L10	L8 and l2	15
☐	L11	514/30	422
☐	L12	L11 and l2	28
☐	L13	514/450	1077
☐	L14	L13 and l2	18
☐	L15	L14 and l3	11
☐	L16	l3 and l12	12

END OF SEARCH HISTORY

Hit List

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Search Results - Record(s) 1 through 7 of 7 returned.

☑ 1. Document ID: US 4831016 A Relevance Rank: 78

L7: Entry 7 of 7 File: USPT May 16, 1989

DOCUMENT-IDENTIFIER: US 4831016 A
TITLE: Reduced avermectin derivatives

Abstract Text (1):
There are disclosed novel avermectin reduction products. The compounds are prepared by selective catalytic hydrogenation of avermectin-like compounds or by reaction of selected double bonds with electrophylic reagents. The reduced avermectin compounds have utility as anti-parasitic agents and compositions for that use are also disclosed. The compounds are also highly potent insecticides against agricultural pests. The reduced avermectin compounds have increased stability towards light which prolongs their insecticidal activities when applied to field crops subject to irradiation by sunlight.

Brief Summary Text (2):
The term avermectin (previously referred to as C-076) is used to describe a series of compounds isolated from the fermentation broth of an avermectin producing strain of Streotomyces avermitilis and derivatives thereof. The morphological characteristics of the culture are completely described in U.S. Pat. No.4,310,519. The avermectin compounds are a series of macrolides, each of which is substituted thereon at the 13-position with a 4'(.alpha.-L-oleandrosyl)-.alpha.-L-oleandrose group. The avermectin compounds and the instant derivatives thereof have a very high degree of anthelmintic and anti-parasitic activity.

Brief Summary Text (3):
Also included in the prior art are certain synthetically modified avermectins such as 22,23-dihydro avermectin B1a/B1b also known as ivermectin disclosed in U.S. Pat. No. 4199569.

Brief Summary Text (4):
The avermectin series of compounds, which are isolated from a fermentation broth, have the following structure: ##STR1## wherein R is the 4'-(.alpha.-L-oleandrsyl)-.alpha. -L-oleandrose group of the structure: ##STR2## and wherein the broken line indicates a single or a double bond; R.sub.1 is hydroxyl and is present only when said broken line indicates a single bond;

Brief Summary Text (7):
There are eight differnet major avermectin natural product compounds and they are given the designations A1a, A1b, A2a, A2b, B1a, B1b, B2a and B2b based upon the structure of the individual compounds.

Brief Summary Text (8):
In the foregoing structural formula, the individual avermectin compounds are as set

forth below (The R group is 4'(.alpha.-L-oleandrosyl)-.alpha.-L-oleandrose):

Brief Summary Text (9):
The avermectin compounds are generally isolated as mixtures of a and b components. Such compounds differ only in the nature of the R.sub.2 substituent and the minor structural differences have been found to have very little effect on the isolation procedures, chemical reactivity and biological activity of such compounds.

Brief Summary Text (12):
The instant invention is concerned with certain derivatives of avermectin compounds wherein the 8,9 double bond and/or the 10,11 double bond is reduced either chemically or by catalytic hydrogenation to prepare a single bond at such positions where such single bond may optionally contain additional substituents. Thus it is an object of the instant invention to describe such reduced avermectin compounds. A further object is to describe processes for the preparation of such compounds. A still further object is to describe the uses of such compounds as anti-parasitic and insecticidal agents. Still further objects will become apparent from a reading of the following description.

Brief Summary Text (52):
The compounds of the instant invention differ from other avermectin compounds in that one or both of the 8,9 or 10,11 double bonds is reduced. The effect of reducing the 8,9 and/or 10,11 double bonds is that the conjugated diene system is broken. The elimination of the conjugated double bonds has a considerable effect on the ultraviolet absorption characteristics of the molecule and has resulted in a surprising and very significant increase in the stability of the molecule when it is exposed to ultraviolet light, as well as ordinary sunlight which has a significant component of ultraviolet light. This increased stability in the presence of ultraviolet light makes these compounds particularly suited to aqricultural applications and also to topical animal applications where photoinstability would be detrimental to the optimum performance of each compound.

Brief Summary Text (53):
The 8,9 and 10,11 double bonds of the avermectin starting materials are either reduced catalytically or are chemically modified. The catalytic reduction is carried out using Platinum group metals as catalysts such as platinum, palladium, rhodimm, and the like. Generally, the metal catalyst is dispersed on and supported on a substrate such as powdered carbon. The reaction is carried out under a blanket of hydrogen gas either at atmospheric pressure or pressurized up to 10 atmospheres (gauge) of hydrogen pressure in pressurable equipment ordinarily used for such reactions. The reaction is carried out in a solvent which is stable to the hydrogenation conditions and which will not adversely affect the catalyst. Lower alkanols, such as methanol, ethanol, isopropanol and the like, ethyl acetate, cyclohexane, and the like are suitable. The reaction is generally carried out at room temperature although temperature as high as 50.degree. C. are suitable and under such conditions the reaction is complete in from 1 to 24 hours. If the hydrogenation apparatus is so equipped, the progress of the reaction may be followed by observing the amount, either in volume or in pressure drop, of hydrogen that is consumed. The products are isolated using techniques known to those skilled in the art.

Brief Summary Text (54):
The catalytic hydrogenation process generally yields a mixture of Products since the avermectin starting materials have three or four double bonds which may be hydrogenated. This would include the 3,4 and 22,23 double bonds. The 14,15 double bond is sterically hindered and generally requires more vigorous reaction conditions than are described above in order to effect hydrogenation. The various hydrogenation products are isolated from the mixture of reaction products using standard techniques such as fractional crystallization and chromatography. The double bonds which are desired to be retained in the final Product may be protected

to render them inert during the hydrogenation procedure. When the hydrogenation is complete, the double bond may be regenerated by removing the protecting groups.

Brief Summary Text (59):
The ultimate starting materials for the compounds of this invention are the avermectin fermentation products defined above which have the isopropyl or sec-butyl group at the 25-position. These compounds with a methyl or ethyl group at the 25-position and no carbohydrate function at the 13-position are often referred to as milbemycin compounds and are disclosed in U.S. Pat. No.3,950,360 to Aoki et al. Thus it is apparent that additional reactions are required to prepare many of the immediate starting materials for the instant compounds. Specifically, reactions are carried out at the 4", 13, 22, and 23-positions. In addition, during the various reactions described above, and below it may be advisable to protect various reactive groups to prevent the undesired reaction of such groups. In addition, protection of such reaction groups may facilitate the separation of the various products. With the appropriate positions protected, the hydrogenation reaction and the other reactions may be carried out without affecting the remainder of the molecule. Following the described reactions, the protecting groups may be removed and the unprotected product isolated. The protecting groups employed is ideally one which may be readily synthesized, will not be affected by the reaction with the various reagents employed and may be readily removed without affecting any other functions of the molecule. It is noted that the instant protected compounds are novel and have considerable antiparasitic activity. They are included within the ambit of the instant invention. One preferred type of protecting group for the avermectin and milbemycin type of molecule is the tri-substituted silyl group, preferably the trialkyl silyl group. One especially preferred example, is the t-butyl dimethylsilyl group. The reaction preparing the protected compound is carried out by reacting a hydroxy compound with the appropriately substituted silylhalide, preferably the silylchloride in an aprotic polar solvent such as dimethylformamide. Imidazole is added as a catalyst. The reaction is complete in from 1 to 24 hours at from 0 to 25.degree. C. For the 5-position hydroxy group the reaction is complete in from 1/2 to 3 hours at from 0.degree. C. to room temperature. This reation is selective to the 5 position under the conditions above described and very little, if any, silylation is observed at other hydroxy substituted positions.

Brief Summary Text (61):
Another of the starting materials used in the foregoing reaction scheme are those in which the 22,23 double bond of the A1 and B1 compounds has been reduced to a single bond. As is readily apparent from an analysis of the structure of avermectin starting materials there are 5 unsaturations in the "1"-series of compounds. Thus in the "1" series of compounds it is possible to selectively reduce the 22,23 double bond while not affecting the remaining four unsaturations or any other functional group present on the molecule. It is necessary to select a specific catalyst for the hydrogenation, one that will selectively hydrogenate the least hindered from among a series of unsaturations. The preferred catalyst for such a selective hydrogenation procedure is one having the formula:

Brief Summary Text (65):
The reaction conditions which are generally applicable to the preparation of both the mono-saccharide and aglycone involve dissolving the avermectin compound or the hydrogenated avermectin compound in an aqueous acidic non-nucleophilic organic solvent, miscible with water, preferably dioxane, tetrahydrofuran, dimethoxyethane, dimethylformamide, bis-2-methoxyethyl ether, and the like, in which the water concentration is from 0.1 to 20% by volume. Concentrated acid is added to the aqueous organic solvent to the extent of 0.01 to 10% by volume. The reaction mixture is generally stirred at about 20.degree.-40.degree. C., preferably at room temperature, for from 6 to 24 hours. The lower concentration of acid, from about 0.01 to 0.1% will predominately produce the monosaccharide under the above reaction conditions. Higher acid concentrations, from about 1 to 10% will predominantly produce the aglycone under the above reaction conditions. Intermediate acid

concentrations will generally produce mixtures of monosaccharide and aglycone. The Products are isolated, and mixtures are separated by techniques such as column, thin layer preparative and high pressure liquid chromatography, and other known techniques.

Brief Summary Text (67):
A further procedure for the preparation of the monosaccharide or aglycone of the avermectin compounds or of the hydrogenated avermectin compounds utilizes a different solvent system for the mono-saccharide and the aglycone. The procedure for the preparation of the monosaccharide uses 1% acid by volume in isopropanol at from 20.degree.-40.degree. C., preferably room temperature, for from 6 to 24 hours. For the preparation of the aglycone, 1% acid, by volume, in methanol under the foregoing reaction conditions has been found to be appropriate.

Brief Summary Text (70):
It has also been observed that the mono-saccharide is prepared during the course of the reaction used to remove the trialkylsilyl protecting group. Since acid catalysis is used to remove the protecting group, this is expected. However, in such cases, both the desired product and the monosaccharide are prepared and they can be readily separated using the above-described techniques.

Brief Summary Text (71):
In the preparation of the 4' or 4" keto or amino substituted compounds, the avermectin starting materials are oxidized at the 4"-position to the corresponding keto compound. The procedures for the preparation of such compounds are described in U.S. Pat. No. 4427663 to Mrozik. During the procedure the presence of any hydroxy groups at the 5 and 23-position will require that such hydroxy groups be protected in order that they too are not oxidized. The 7-hydroxy group is very unreactive and need not be protected. The procedure used to prepare the protected intermediates are described above. The oxidation reaction is carried out in an inert solvent such as methylene chloride using oxalyl chloride or trifluoroacetic anhydride in dimethylsulfoxide as the oxidizing agent. Additionally N-chlorosuccinimide in dimethylsulfide may be employed. The reaction proceeds by dissolving the oxalyl chloride or trifluoroacetic anhydride and dimethylsulfoxide (or other oxidizing reagents) in methylene chloride and cooling to from -50.degree. to -80.degree. C. and adding dropwise a methylene chloride solution of the avermectin compound to be oxidized. The addition is carried out over a period of from 15 minutes to 1 hour and then triethylamine is added dropwise over a period of from 1 to 15 minutes. The reaction mixture is then allowed to warm to room temperature over a period of from 1/2 to 1 hour. The 4' or 4"-keto compound is isolated using techniques known to those skilled in the art.

Brief Summary Text (74):
The substitution reaction wherein the substituent is an acyl function is carried out using an acylating reagent in the presence of a base in an inert solvent. The acylation of avermectin compounds, is fully described in U.S. Pat. No. 4201861 to Mrozik et al. The preferred acylating reagents are loweralkanoyl anhydrides, lower alkanoyl halides, substituted benzene sulfonyl chlorides, lower alkyl sulfonyl chlorides, and the like. The reaction is carried out in an inert solvent such as methylene chloride in the presence of a non-reactive base such as pyridine or triethylamine in order to neutralize the acid produced during the course of the reaction. The reaction temperature is from -10.degree. to 25.degree. C. and the reaction is complete in from 5 minutes to 8 hours. The product is isolated using known techniques.

Brief Summary Text (75):
The reaction for the preparation of the 4' or 4"-deoxy-4'- or 4"-dialkylamino compounds is carried out using the alkylating reaction conditions of an excess of a carbonyl compound, preferably formaldehyde and a reducing agent such as sodium cyano borohydride, in methanol. The reaction is carried out in a solvent suitable

to dissolve the organic starting material using excess aqueous formaldehyde along with the presence of a small amount of acid such as acetic acid to facilitate the reaction. The reaction is carried out at from -10.degree. to +25.degree. C. with the solution of the avermectin compound in methanol added dropwise over a period of from 30 to 60 minutes to the alkylating reagent mixture and the product is isolated using known techniques.

Brief Summary Text (76):
Further reactions of the avermectin compounds either before or after the reduction reaction are possible to prepare the compounds of this invention. The double bonds at 3,4; 8,9; and 10,11 may be converted to epoxides using the procedures described in U.S. Pat. No. 4530921 to Mrozik. The procedures described in said reference are specifically directed to the 8,9 and 14,15 double bonds. However, they are equally applicable to the other double bonds identified above. The reaction is carried out with a mild oxidizing agent such as m-chloroperbenzoic acid, t-butyl hydroperoxide, catalyzed with vanadyl acetylacetonates, and the like. Where more than one double bond is epoxidized, the various products are readily separated using fractional crystallization and chromatographic techniques.

Brief Summary Text (79):
The various hydroxy groups, such as at 5, 13, 23, 4' and 4" may be alkylated following the procedures described in U.S. Pat. No. 4200581 to Fisher et al. The preparation of 13-(alkoxy)methoxy avermectin aglycone derivatives is described in U.S. Pat. No. 4,587,247.

Brief Summary Text (81):
The disease or group of diseases described generally as helminthiasis is due to infection of an animal host with parasitic worms known as helminths. Helminthiasis is a prevalent and serious economic problem in domesticated animals such as swine, sheep, horses, cattle, goats, dogs, cats and poultry. Among the helminths, the group of worms described as nematodes causes widespread and often times serious infection in various species of animals. The most common genera of nematodes infecting the animals referred to above are Haemonchus, Trichostrongylus, Ostertagia, Nematodirus, Cooperia, Ascaris, Bunostomum, Oesophagostomum, Chabertia, Trichuris, Strongylus, Trichonema, Dictyocaulus, Capillaria, Heterakis, Toxocara, Ascaridia, Oxyuris, Ancylostoma, Uncinaria, Toxascaris, and Parascaris. Certain of these, such as Nematodirus, Cooperia and Oesphagostomum attack primarily the intestinal tract while others, such as Haemonchus and Ostertagia, are more prevalent in the stomach while still others such as Dictyocaulus are found in the lungs. Still other parasites may be located in other tissues and organs of the body such as the heart and blood vessels, subcutaneous and lymphatic tissue and the like. The parasitic infections known as helminthiases lead to anemia, malnutrition, weakness, weight loss, severe damage to the walls of the intestinal tract and other tissues and organs and, if left untreated, may result in death of the infected host. The substituted avermectin compounds of this invention have unexpectedly high activity against these parasites, and in addition are also active against Dirofilaria in dogs, Namatospiroides, Syphacia, Aspiculuris in rodents, arthropod ectoparasites of animals and birds such as ticks, mites, lice, fleas, blowfly, in sheep Lucilia sp., biting insects and such migrating diperous larvae as Hypoderma sp. cattle, Gastrophilus in horses, and Cuterebra sp. in rodents.

Brief Summary Text (86):
Where it is desired to administer the avermectin derivatives in a dry, solid unit dosage form, capsules, boluses or tablets containing the desired amount of active compound usually are employed. These dosage forms are prepared by intimately and uniformly mixing the active ingredient with suitable finely divided diluents, fillers, disintegrating agents and/or binders such as starch, lactose, talc, magnesium stearate, vegetable gums and the like. Such unit dosage formulations may be varied widely with respect to their total weight and content of the antiparasitic agent depending upon factors such as the type of host animal to be

treated, the severity and type of infection and the weight of the host.

Brief Summary Text (87):
When the active compound is to be administered via an animal feedstuff, it is intimately dispersed in the feed or used as a top dressing or in the form of pellets which may then be added to the finished feed or optionally fed separately. Alternatively, the antiparasitic compounds of our invention may be administered to animals parenterally, for example, by intraruminal, intramuscular, intratracheal, or subcutaneous injection in which event the active ingredient is dissolved or dispersed in a liquid carrier vehicle. For parenteral administration, the active material is suitably admixed with an acceptable vehicle, preferably of the vegetable oil variety such as peanut oil, cotton seed oil and the like. Other parenteral vehicles such as organic preparation using solketal, glycerol formal, and aqueous parenteral formulations are also used. The active avermectin compound or compounds are dissolved or suspended in the parenteral formulation for administration; such formulations generally contain from 0.005 to 5% by weight of the active compound.

Brief Summary Text (91):
Such supplements are added to the animal feed in an amount to give the finished feed the concentration of active compound desired for the treatment and control of parasitic diseases. Although the desired concentration of active compound will vary depending upon the factors previously mentioned as well as upon the particular avermectin derivative employed, the compounds of this invention are usually fed at concentrations of between 0.00001 to 0.002% in the feed in order to achieve the desired antiparasitic result.

Brief Summary Text (92):
The avermectin compounds of this invention are also useful in combatting agricultural pests that inflict damage upon crops while they are growing or while in storage. The compounds are applied using known techniques as sprays, dusts, emulsions and the like, to the growing or stored crops to effect protection from such agricultural pests.

Brief Summary Text (93):
In using the compounds of this invention, the individual substituted avermectin components may be prepared and used in that form. Alternatively, mixtures of two or more of the individual avermectin components may be used, as well as mixtures of the parent avermectin compounds, other avermectin compounds or other active compounds not related to avermectin, with the compounds of this invention.

Brief Summary Text (94):
In the isolation of the avermectin compounds, which serve as starting materials for the instant processes, from the fermentation broth, the various avermectin compounds will be found to have been prepared in unequal amounts. In particular an "a" series compound will be prepared in a higher proportion than the corresponding "b" series compound. The difference between the "a" series and "b" series is constant throughout the avermectin compounds and consists of a sec-butyl group and an iso-propyl group respectively at the 25 position. This difference, of course, does not interfere with any of the instant reactions. In particular it may not be necessary to separate the "b" components from the related "a" component. Separation of these closely related compounds is generally not practiced since the "b" compound is present only in a small percent by weight, and the structural difference has negligible effect on the reaction processes and biological activities.

Brief Summary Text (95):
ln particular it has been found that the starting materials for the compounds of this invention are very often prepared in a ratio of about 80% avermectin B1a or A1a and 20% avermectin B1b or A1b. Thus the preferred composition of this invention

is one which contains about 80% of the "a" component and 20% of the "b" component.

Brief Summary Text (97):
The substituted avermectin derivatives prepared in the following examples are generally isolated as amorphous solids and not as crystalline solids. They are thus characterized analytically using techniques such as mass spectrometry, nuclear magnetic resonance, and the like. Being amorphous, the compounds are not characterized by sharp melting points, however, the chromatographic and analytical methods employed demonstrate the purity of the compounds.

Brief Summary Text (98):
In the following examples, the various starting materials therefor are avermectin compounds or derivatives of avermectin compounds. The avermectin compounds and the preparation and isolation thereof from fermentation broths are described in U.S. Pat. No. 4,310,519 issued 12 January 1982. The selective 22,23-dihydro derivatives of avermectin compounds are described in U.S. Pat. No. 4,199,569. The aglycone and monosaccharide derivatives of avermectin compounds are described in U.S. Pat. No. 4,206,205. The 13-deoxy compounds are described in U.S. Pat. Nos. Re 32006aand Re 32034. The milbemycin compounds are described in U.S. Pat. No. 3,950,360. The 4' and 4" amino compounds are described in U.S. Pat. No. 4,427,663. The acyl derivatives are disclosed in U.S. Pat. No. 4201861. The epoxide derivatives are disclosed in U.S. Pat. No. 4,530,971. The 13-keto and amino compounds are disclosed in U.S. Pat. No. 4,579,864, and the o-alkyl compounds are disclosed in U.S. Pat. No. 4,200,581. The 13-(alkoxy)methoxy compounds are disclosed in U.S. Pat. No. 4,587,247. The following examples are being provided in order that the invention may be more fully understood. They are not to be construed as being limitative of the invention.

Detailed Description Text (3):
A solution of 7.25 g of avermectin B1a/B1b in 60 mL of N,N-dimethylformamide was stirred with 3 mL of t-butyldiphenylsilyl chloride, 1.5 g imidazole, and 100 mg N,N-dimethylaminopyridine at room temperature for 48 hours. The reaction was stopped by addition of water and extraction with dichloromethane afforded the product as an oil. High performance liquid chromatography (HPLC) on silica gel using 842 1.4:3 (v:v) ethylacetate: hexane provided 7.7 g purified 5-O-t-butyl-diphenylsilylavermectin-B1a/B1b as a foam, characterized by its .sup.1 H NMR spectrum.

Detailed Description Text (5):
5-O-tert-Butyldiphenylsilyl-10,11,22,23-tetrahydro avermectin B1a/B1b.

Detailed Description Text (6):
A solution of 1.1 g 5-O-tert-butyldiphenylsilyl avermectin B1a/B1b in 10 mL of absolute ethanol and 0.2 g of 5% palladium on carbon was shaken in a Parr hydrogenator with hydrogen at 90 pounds pressure at room temperature until the drop in pressure indicated the uptake of one molar equivalent. The hydrogenation was stopped and a small sample was withdrawn for analysis. High performance liquid chromatographic analysis on a reverse phase C.sub.18 column with a methanol-water liquid phase indicated the major components to be the 5-O-tert-butyldiphenylsilyl-22, 23-dihydroavermectin-B1a/B1b. The Parr hydrogenator was charged with another 0.2 g 5% Pd/C and the system repressurized to 84 lbs with hydrogen. After another pressure drop indicated the uptake of another molar equivalent of hydrogen, the catalyst was removed by filtration. Evaporation of the filtrate afforded a mixture of which the title compound is a major component. HPLC purification with a preparative reverse phase C18 column using a methanol-water liquid phase affords 5-O-tert-butyl-diphenylsilyl-10,11,22,23-tetrahydro avermectin B1a/B1b as an amorphous solid characterized by its .sup.1 H NMR and mass spectrum.

Detailed Description Text (14):
A solution of 870 mg avermectin B2a/B2b in 25 mL of absolute ethanol and 100 mg of

5% Pd/C was stirred at room temperature under one atmosphere pressure of hydrogen. After an uptake of 1.5 molar equivalent of hydrogen, the catalyst was removed by filtration. HPLC analysis using a reverse Phase C.sub.18 column and a methanol-water liquid system indicated the composition of the mixture to be 20% avermectin B2a/B2b, 50% 10,11-dihydroavermectin B2a/B2b, 30% 3,4-dihydroavermectin B2a/B2b, and 10% 3,4,10,11-tetrahydroavermectin B2a/B2b. Preparative HPLC using a reverse Phase C.sub.18 column and a methanol-water system followed the separation and characterization of each of the titled compounds via their 1H NMR and mass spectra.

Detailed Description Text (32):
Desilylation of 60 mg of the compound of Example 10 following the procedure established by Example 3 furnished 22 mg of 4"-amino-4"-deoxy-10,11,22,23-tetrahydro avermectin B1a/B1b as an amorphous solid characterized by its 1H NMR (200MHz, CDCl.sub.3 TMS) 3.08 ppm (br S, 1H) for C-4"H and mass spectrum for 4"-epiamino-4"-deoxy-10,11,22,23, tetrahydroavermectin B.sub.1 a, C.sub.48 H.sub.77 O.sub.13 N, calculated 875.5395, found 875.5396.

Detailed Description Text (35):
Avermectin A2/A2b aglycone is reacted under the conditions of experiment 6 to give 10,11-dihydroavermectin A2a/A2b aglycone.

Detailed Description Text (38):
Avermectin B1a/B1b aglycone is subjected to the catalytic hydrogenation conditions detailed in example 6 to give 10,11,22,23-tetrahydroavermectin B1a/B1b aglycone.

Detailed Description Text (41):
To 380 mg avermectin B1a/B1b in 9 mL of acetone and 1 mL of water was added 100 mg of N-bromoacetamide. The mixture was stirred in the dark at room temperature for 1 hour and work up consists of addition of water and extraction with dichloromethane. The solvent was removed in vacuo and the residual solid purified by preparative thick layer silica gel chromatography using a ethylacetate-hexane solvent system to afford 80 mg of 10,11-dihydro-11-bromo-10-hydroxyavermectin B1a/B1b as an amorphous solid characterized by its 1H NMR spectrum.

Detailed Description Text (43):
10,11-Dihydro-11-bromo-10-hydroxy-4",5di-O-t-butyldimethylsilyl avermectin B1a/B1b

Detailed Description Text (48):
EXAMPLE 17 0,11-Dihydro-10-hydroxy-4", 5-di-O-tert-butyldimethylsilyl avermectin B1a/B1b

Detailed Description Text (51):
10,11-Dihydro-10-oxo-4", 5-di-O-tert-butyldimethylsilyl avermectin B1a/B1b

Detailed Description Text (52):
Starting with the compound from Example 17 following the Swern oxidation procedure established by Example 9, the 10-hydroxy function was oxidized to a ketone obtained as an amorphous solid characterized by its 1H-NMR spectrum as 10,11-dihydro-10-oxo-4", 5-di-O-tert-butyldimethylsilyl avermectin B1a/B1b.

Detailed Description Text (54):
10, 11-Dihydro-10-oxo-avermectin B1a/B1b

Detailed Description Text (55):
The compound from Example 18 was desilylated with hydrogen fluoride-pyridine following the procedure of Example 3 to provide an amorphous solid characterized by its 1H NMR and mass spectrum as 10,11-dihydro-10-oxo-avermectin B1a/B1. The mass spectrum for 10,11-dihydro-10-oxoavermectin B1a was calculated at 852.4660 and found as 852.4656 (for M.sup.+ less two water). The nuclear magnetic resonance